EXHIBIT V

ETHICON, INC.
a Johnson & Johnson company

P.O. BOX 151
SOMERVILLE, NEW JERSEY 08876-0151

May 26, 2000

To: P. Cecchini

Re: Review of Biocompatibility Data on the Tension Free Vaginal Tape (TVT) System for Compliance to FDA G-95/ ISO 10993/ EN 30993

The Tension Free Vaginal Tape (TVT) System is composed of a polypropylene mesh covered by a polyethylene sheath, and attached to a stainless steel needle using polyolefin shrink tubing. The polypropylene mesh is made from the same raw material as PROLENE* polypropylene suture.

The polypropylene mesh used in this system is a permanent tissue implant. FDA G-95[1]/ ISO 10993/ EN 30993[2] require the following potential biological effects be considered for implants with permanent exposure to patient tissues: Cytotoxicity, Sensitization, Irritation/ Intracutaneous Reactivity, Acute Systemic Toxicity, Subchronic Toxicity, Genotoxicity, Implantation, Chronic Toxicity, and Carcinogenicity. The long history of clinical use of PROLENE meshes and sutures combined with safety data generated for PROLENE sutures and confirmatory cytotoxicty testing on this product demonstrate the safety of this material. The results of cytotoxicity testing of TVT PROLENE mesh are reviewed in the attached memo[3]. Based on acceptable tissue reaction of PROLENE sutures[4] and the long history of safe clinical use of polypropylenes and PROLENE suture, no additional implantation or irritation data was considered necessary. Based on acceptable chronic toxicity assessment of PROLENE sutures and the long history of safe clinical use of polypropylenes and PROLENE suture, no additional Acute Systemic Toxicity, Sensitization, Subchronic Toxicity or Chronic Toxicity data was considered necessary. Based on acceptable Carcinogenicity assessment of PROLENE sutures and the long history of safe clinical use of polypropylenes and PROLENE suture no additional Genotoxicity or Carcinogenicity data was considered necessary.

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* TRADEMARK
[1] FDA General Program Memorandum #G95-1: Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices.
[2] ISO 10993/ EN 30993: Biological Evaluation of Medical Devices
[3] Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device, T.A. Barbolt (8-8-1997)
[4] Corporate Product Characterization Product Safety Profile for PROLENE polypropylene suture (5-26-00)

The polyethylene sheath, stainless steel needle, and polyolefin shrink tubing used in this system have transient contact with patient tissues. FDA G-95/ ISO 10993/ EN 30993 do not specifically address this type of patient contact. After reviewing the chemical nature of the materials, and potential patient contact, it was concluded that cytotoxicity testing was sufficient to assure safety. The results of cytotoxicity testing of the components are reviewed in the attached memo[5].

In conclusion, the biocompatibility data available for the TVT system is considered to be sufficient to satisfy the requirements of FDA G-95, ISO 10993, and EN 30993.

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Senior Scientist
Preclinical Safety Assessment
Corporate Product Characterization, Ethicon R&D

cc: T. Barbolt
L. Traver→ CPC CF
RDCF

[5] Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device, T.A. Barbolt (8-8-1997)

ETHICON, INC.
a Johnson & Johnson company
P.O. BOX 151
SOMERVILLE • NEW JERSEY • 08876-0151

August 8, 1997

To: C. Linsky

Re: Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device

A number of in vitro cytotoxicity studies were conducted to assess the cytotoxic potential of the components of the Ulmsten device as part of an overall assessment of biocompatibility (Attachment 1). The device consists of two stainless steel needles, a polyethylene (PE) sheath, heat-shrink tubing (connects mesh and sheath to needle), two PE needle guards, and a strip of polypropylene (PP) mesh. The needles, heat-shrink tubing, and the PE sheath have relatively brief contact with the patient while the PP mesh is permanently implanted in the body. The PE needle guards are used to prevent the needles from damaging the packaging and do not come in contact with the patient.

The testing was conducted at different locations using testing protocols that varied in some important aspects such as extraction conditions and scoring systems. After an evaluation of all the test results, the components of the Ulmsten device that were considered to be "noncytotoxic" were the needle, PE needle guard, heat-shrink tubing, and PE sheath. Overall, there is some evidence to suggest that the PP mesh from the sterile Ulmsten device may have cytotoxic potential. However, the raw material PP mesh was considered to be noncytotoxic.

The assessment of biocompatibility of a medical device must take into consideration all available data including clinical data which is the most relevant. In this case, there is abundant clinical data (around 1000 patients including over 200 documented cases) which demonstrates that the Ulmsten PP mesh strip implanted in the body to control urinary stress incontinence has fewer complications in terms of tissue reaction than other comparable devices. This suggests that any potential irritancy of the PP mesh after implantation is self-limiting and minimal when compared to the implantation procedure itself. Thus, this clinical data provides important evidence that the cytotoxicity of the PP mesh observed in vitro does not translate into any clinical significance or adverse patient outcomes.

Thomas A. Barbolt, Ph.D., D.A.B.T.
Research Fellow
Corporate Product Characterization

cc: S. Liu
P. Cecchini
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Attachment 1

Summary of Cytotoxicity Testing

1. Scantox Study

The initial cytotoxicity testing of the finished Ulmsten device was conducted by Scantox (Lab No. 22806) for Medscand Medical AB during March 10-13, 1997. This testing was limited to an ISO Elution test of the heat-shrink tubing (3 cm^2/ml including both sides) and PE sheath (6 cm^2/ml including both sides) components after extraction together for 24 hours at 37 °C. The results (on the USP scoring scale of 0 to 4) indicated that the extract was severely (grade 4) cytotoxic. These test results are considered inconclusive because the extracts of these materials were tested together.

2. Ethicon, Scotland Studies

A series of cytotoxicity experiments were then conducted by Ethicon, Scotland (Interim Report 15/97) during early May, 1997 to expand on the results from the Scantox study. The results (on an internal scoring scale of 0 to 3) of the ISO Elution test of the sterile Ulmsten device components extracted for 24 hours at 37 °C were as follows:

Needle (0.1 g/ml) - Noncytotoxic
Heat-shrink tubing (0.1 g/ml) - Marked cytotoxicity
PE sheath (3 cm^2/ml [includes only one side]) - Slight cytotoxicity
PP mesh (3 cm^2/ml [includes only one side]) - Marked cytotoxicity

In addition, cytotoxicity testing was conducted under similar conditions on sterile and nonsterile samples of PP mesh used in the construction of the Ulmsten device. The results indicated that these PP mesh samples also had marked cytotoxicity.

The results of ISO Agar Overlay test (on an internal scoring scale of 0 to 3) of the device components were as follows:

Heat-shrink tubing - Moderate cytotoxicity
PE sheath - Slight cytotoxicity
PP mesh - Marked cytotoxicity

3. BIOLAB, Italy Studies

Further cytotoxicity testing of the sterile Ulmsten device was conducted by BIOLAB, Italy (Report Nos. 97/8053-1, 97/8053-2, 97/8053-3) in early June, 1997. The results (on a USP

scoring scale of 0 to 4) of the ISO Elution test of the device components extracted (by weight) for 72 hours at 37 °C were as follows:

Heat-shrink tubing (0.2 g/ml) - Noncytotoxic
PE sheath (0.2 g/ml) - Slight cytotoxicity
PP mesh (0.2 g/ml) - Noncytotoxic

4. NAmSA, U.S. Studies

Final testing of the sterile Ulmsten device was conducted by NAmSA, U.S. (PSE 97-0128) in early July, 1997 to provide cytotoxicity results from a laboratory which has been used reliably by Ethicon, Inc. for a number of years to support regulatory submissions and for which there is a baseline of cytotoxicity data for a number of our products. The results (on a USP scoring scale of 0 to 4) of the ISO Elution test of the device components extracted for 24 hours at 37 °C were as follows:

Heat-shrink tubing (3 cm^2/ml [includes both sides]) - Noncytotoxic
PE sheath (6 cm^2/ml [includes both sides]) - Noncytotoxic
PE needle guard (3 cm^2/ml) - Noncytotoxic
Needle (0.2 g/ml) - Noncytotoxic
PP mesh (3 cm^2/ml [includes both sides, 33 mg/ml]) - Severe cytotoxicity

The results of ISO Agarose Overlay testing for the device components were as follows:

Heat-shrink tubing - Noncytotoxic
PE sheath - Noncytotoxic
PP mesh - Noncytotoxic

In addition, ISO Elution cytotoxicity testing was conducted under similar conditions at NAmSA on two of the same nonsterile samples of PP mesh which resulted in marked cytotoxicity in tests conducted at Ethicon (Scotland). The results (PSE 97-0122 and 97-0123) indicated that these PP mesh samples were noncytotoxic.

Discussion

To gain a broader perspective of the cytotoxicity of PP devices in general, elution cytotoxicity studies were also conducted with Bard Marlex PP mesh (PSE 97-0118) and Surgilene PP suture (PSE 97-0119). The results indicated that these PP devices were noncytotoxic. Also, Ethicon, Inc. conducted agarose overlay and elution cytotoxicity tests with normal production sterile PROLENE (polypropylene) mesh at NAmSA in 1993 (PTS 92-1411) which indicated that this PP mesh was noncytotoxic in both cytotoxicity test systems. It should be noted that PP is often used in cytotoxicity testing as a negative control as it was in the first study conducted by Scantox.

Some of the apparent conflicting test results from the different testing facilities can be addressed by understanding that slightly differing testing protocols were followed. Although all the testing was described as conforming to ISO 10993-5 guidelines entitled "Biological Evaluation of Medical Devices - Tests for Cytotoxicity: In Vitro Methods", there were some technical differences relating to the extraction procedures, all within the broad guidelines of this standard, which may have influenced the final outcomes.

For example, USP extraction conditions state that both sides of a two-dimensional sample (e.g. mesh) be included in the calculation of surface area for extraction. Since Ethicon (Scotland) used only one side in the calculation of surface area, they effectively doubled the amount of material extracted compared to the testing conducted at NAmSA. Thus, the test results from NAmSA for the samples of raw material PP mesh used in the construction of the Ulmsten device indicating no cytotoxicity were considered to most appropriately reflect the potential cytotoxicity of this material.

Using the USP acceptability criteria for cytotoxicity to be a grade of no more than mild (Grade 2) cytotoxicity, the components of the Ulmsten device found to be "noncytotoxic" were the needle, PE needle guard, and PE sheath. The heat-shrink tubing was found to be noncytotoxic by NAmSA and BIOLAB. The moderate to marked cytotoxicity of the heat-shrink tubing reported by Ethicon (Scotland) may be a reflection of the different scoring system and/or the increased sensitivity of the test systems. However, based on the weight of the evidence, the heat-shrink tubing was considered to be noncytotoxic.

The PP mesh component of the Ulmsten device was cytotoxic in only the Elution test reported by NAmSA and in both test sytems reported by Ethicon (Scotland). The noncytotoxic result reported from BIOLAB is not clearly understood. Although the extraction conditions were exaggerated (200 mg/ml versus 33 mg/ml and 72 hours versus 24 hours), no information is available on the stability of this extract over time. Overall, there is some evidence to suggest that the PP mesh from the sterile Ulmsten device may have cytotoxic potential.

Conclusion

An assessment of the biocompatibility of a medical device must take into consideration all available data, including clinical data which is the most relevant, rather than focus on individual test results. In this case, there is abundant clinical data (around 1000 patients including over 200 documented cases) which demonstrates that the Ulmsten PP mesh strip implanted in the body to control urinary stress incontinence has fewer complications in terms of tissue reaction than other comparable devices. This suggests that any potential irritancy of the PP mesh after implantation is self-limiting or minimal when compared to the implantation procedure itself. Thus, this clinical data provides important evidence that the cytotoxicity of the PP mesh observed in vitro does not translate into any clinical significance or adverse patient outcomes.

CORPORATE PRODUCT CHARACTERIZATION

Product Safety Profile
(Updated 5/26/00)

A. PRODUCT

PROLENE* polypropylene suture, monofilament, synthetic, nonabsorbable, dyed (blue) or undyed (NDA 16-374)

B. DESCRIPTION

PROLENE suture is a monofilament synthetic nonabsorbable surgical suture composed of an isotactic crystalline stereoisomer of polypropylene, a linear polyolefin. PROLENE suture has no true coating but does possess a small amount of additive which "migrates" to the surface of the suture during its manufacture and acts to reduce tissue drag. This characteristic lack of adherence to tissue makes PROLENE suture efficacious as a pull-out suture. Due to its relative biological inertness, PROLENE suture is recommended for use where the least possible suture reaction is desired and has gained wide acceptance in general, cardiovascular, plastic, and orthopaedic surgery. PROLENE suture is available clear or pigmented blue with copper phthalocyanine and in sizes 11-0 to 2.

C. GENOTOXICITY: Not done

D. CYTOTOXICITY

1. L929 Agar Overlay Test, Elution Assay, and the Clonal Suppression Assay (M83-184)

Report Date: 11/4/83
Test Article: PROLENE suture (control sample) and Ethylene Propylene Suture - Prep (test sample), dyed, size 2-0
Results: The test articles were tested for *in vitro* cytotoxicity using the Agar Overlay Test, Elution Assay, and Clonal Suppression Assay. Cytotoxicity was not observed in the Agar Overlay Test (solids or extracts), the Elution Assay, or the Clonal Suppression Assay. Both materials were considered nontoxic.

2. In Vitro Cytotoxicity - Clear PROLENE Polypropylene Suture, Size 4-0 (ERF 88-0493)

Report Date: 12/16/88
Test Article: PROLENE suture, size 4-0, clear
Results: The test article was evaluated in two *in vitro* assays. In the Agar Overlay Assay, no cytotoxicity to mouse fibroblast cells was observable after exposure to autoclaved or unautoclaved PROLENE suture. In the MEM Elution Assay, cultures of mouse fibroblast cells were exposed to extracts of PROLENE suture. The culture medium extracts of unautoclaved PROLENE suture were somewhat cytotoxic to mouse fibroblast cells after 48 hours of exposure. Autoclaving the samples prior to extraction caused the extracts to become clearly toxic after 24 hours of exposure to the cells and extremely toxic after 48 hours.

E. HEMOCOMPATIBILITY

1. Hemolysis: ULX II Suture (ERF 82-0648)

Report Date: 1/7/83
Test Article: PROLENE suture (comparative control) and ULX II suture, size 2-0, and their saline extracts (0.5 g/10 ml saline)
Results: PROLENE suture and its saline extract produced a hemolysis value of 0% in defibrinated rabbit blood. PROLENE suture was considered nonhemolytic.

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F. PYROGENICITY: Not done

G. TISSUE IRRITATION

1. Sutures Packaged with Permeable Labels: Ethylene Oxide Sterilized (ERF 71-0030)

Report Date: 5/20/71
Test Article: PROLENE suture, size 5-0
Results: The test article was implanted intramuscularly in rats for a period of 3, 14, or 28 days. Median tissue reactions were in the slight range. The tissue reactions throughout the experiment were not considered unusual.

2. Epoxy Tipped NYLON* and PROLENE - Biological Evaluation (ERF 71-0233)

Report Date: 3/3/72
Test Article: PROLENE suture, size 6-0, tipped with epoxy bonding agent containing Eastman 343-1 chlorinated polyolefin, EO sterilized
Results: Samples were implanted intramuscularly in rats for a period of 3, 7, or 28 days. No unusual reactions were observed and responses after one month of implantation were minimal and similar to those elicited by untipped control sutures.

3. PROLENE* Polypropylene Sutures: Tissue Response, Rats (ERF 74-0402)

Report Date:
Test Article: PROLENE suture, sizes 8-0, 9-0, and 10-0
Results: PROLENE suture was implanted in rats intramuscularly for 3, 7, 14, or 28 days. Tissue reaction to all samples was slight at 3 days postimplantation and a minimal foreign body response was observed at 28 days postimplantation.

4. PROLENE (Polypropylene) Sutures: Surface Additive Study - Tissue Response, Rats - Pilot Study: Final Report (ERF 83-0477)

Report Date: 10/19/83
Test Article: PROLENE suture, size 2-0, scoured, then heated to induce excess surface emigration of additives, coated with Santanox R antioxidant, DLTDP antioxidant, Luberol PX plasticizer, calcium stearate, or copper phthalocyanine.
Results: The test articles were implanted into the gluteal muscles of rats to identify specific agents used in the manufacture of PROLENE suture, if any, which might cause adverse responses. Samples were explanted at 3, 14, or 28 days postimplantation. All the PROLENE suture samples, regardless of surface treatment, elicited median tissue response scores in the slight range at each of the postimplantation periods. However, the samples prepared with the Santanox R antioxidant and the Luberol PX plasticizer as surface additives elicited a few individual site responses that were greater than the majority of the responses. This was observed at the 14 day period for the Luberol and both the 14 and 28 day periods for the Santanox. Although not conclusive, these findings warranted further study focusing on the Luberol PX and Santanox R additives.

5. Size 5-0 and 0 PROLENE (Polypropylene): Cobalt and Ethylene Oxide Sterilized: Effects of Sterilization on Tissue Reaction: Final Report (ERF 83-0557)

Report Date: 11/16/83
Test Article: PROLENE suture, sizes 5-0 and 0, Cobalt radiation (2.5 Mrads under nitrogen), or EO sterilization
Results: Samples implanted into the gluteal muscles of rats were recovered at 7, 28, or 91 days. Tissue reactions elicited by the samples were foreign body in type. Median reaction scores were in the slight range

at 7 days and in the near minimal or minimal range at 28 and 91 days. Reaction scores between EO sterilized and Co irradiated PROLENE suture were approximately the same.

6. 11-0 ETHILON* and PROLENE (Polypropylene) - Ocular Tissue Response (ERF 83-0699)

Report Date: 2/29/84
Test Article: ETHILON* nylon suture and PROLENE suture, size 11-0, dyed
Results: Suture samples were implanted into the corneal tissues of New Zealand White Rabbits for a period of 7, 30, or 91 days. PROLENE suture elicited tissue responses entirely in the minimal ranges at the 7 day period, and essentially in the minimal or slight ranges at the 30 and 91 day periods. The tissue responses to PROLENE suture samples consisted primarily of macrophages, and fibroblasts surrounding the sutures. At the 91 day period, there were occasional minimal concentrations of heterophils present.

7. PROLENE (Polypropylene) Suture; New Resin; Tissue Reaction in Rat Gluteal Muscle (ERF 87-0589)

Report Date: 3/29/88
Test Article: PROLENE suture, sizes 7-0 and 2-0, prepared from new resin, using a two-stage draw procedure
Results: New resin PROLENE suture elicited median tissue reaction scores in the minimal or slight range when implanted into the gluteal muscles of rats for a period of 7, 14, 28, 56, or 91 days. Reactions consisted primarily of macrophages and fibroblasts/fibrocytes and occasional minimal concentrations of eosinophils and/or giant cells. Reactions were no different from those elicited by old resin PROLENE suture control samples.

8. PROLENE (Polypropylene) Suture; Procol vs. Lubrol; Tissue Reaction (ERF 88-0326)

Report Date: 3/13/90
Test Article: PROLENE suture, sizes 2-0 and 7-0, dyed, with either an experimental component, Procol, or the standard production component, Lubrol, added to the resin.
Results: Samples were implanted into the gluteal muscles of rats for a period of 7, 14, 28, 56, or 91 days to determine their tissue reaction characteristics. Both test articles elicited median tissue reaction scores in the minimal or slight range. There were no differences among tissue reactions elicited by the test and control samples.

9. PROLENE Sutures: Sizes 4-0 and 7-0; Eto/N_2 Sterilization - Tissue Reaction (ERF 89-0048)

Report Date: 7/6/89
Test Article: PROLENE suture, sizes 4-0 and 7-0, dyed, sterilized by an experimental ethylene oxide/nitrogen process (test sample) or by the ETHICON production ethylene oxide/freon sterilization process (control sample).
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 7, 14, 28, 56, or 91 days. Tissue reactions elicited by the samples were foreign body in type. The median tissue reaction scores for the test samples were in the minimal or slight range throughout the study while the median tissue reaction scores for the control samples were in the slight range at all periods.

10. PROLENE (Polypropylene) Suture; Dyed, 6-0, Stability Study 752 A & B Baseline; Eto/CO_2; Tissue Reaction (ERF 89-0711)

Report Date: 3/15/90
Test Article: PROLENE suture, size 6-0, dyed, sterilized an experimental ethylene oxide/carbon dioxide process (test sample), or by the ETHICON production ethylene oxide/freon sterilization process (control sample), stored in production packaging at ambient conditions for a period of 12 months

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Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. Both test articles elicited median tissue reaction scores in the minimal or slight ranges throughout the study. There were no apparent differences between the test and control samples.

11. PROLENE (Polypropylene) Suture: Dyed, Size 0, Stability Study #749 A & B Baseline: Eto/CO_2: Tissue Reaction (ERF 89-0712)

Report Date: 3/15/90
Test Article: PROLENE suture, size 0, dyed, sterilized by an experimental ethylene oxide/carbon dioxide process (test sample) or by the ETHICON production ethylene oxide/freon sterilization process (control sample).
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. Both samples elicited median tissue reaction scores in the minimal or slight ranges throughout the study. There were no apparent differences between the test and control samples.

12. PROLENE (Polypropylene) Suture: Dyed, Size 0, Stability Study #749 A & B 12- Month Station: Tissue Reaction (ERF 90-0549)

Report Date: 10/18/91
Test Article: PROLENE suture, size 0, dyed, sterilized by an experimental ethylene oxide/carbon dioxide process (test sample) or by the ETHICON production ethylene oxide/freon sterilization process (control sample), stored in production packaging at ambient conditions for a period of 12 months
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. Samples elicited median tissue reaction scores in the very low moderate range at 3 days and in the slight range at 28 and 91 days. There were no apparent differences between the test and control samples, or between the reactions elicited by the baseline (ERF 89-0712) and the 12-month station sutures.

13. PROLENE (Polypropylene) Suture, Dyed, 6-0, Stability Study No. 752 A & B 12- Month Station: Tissue Reaction (ERF 90-0516)

Report Date: 8/14/91
Test Article: PROLENE suture, size 6-0, dyed, sterilized by an experimental ethylene oxide/carbon dioxide process (test sample) or by the ETHICON production ethylene oxide/freon sterilization process (control sample), stored in production packaging at ambient conditions for a period of 12 months
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. Both test articles elicited median tissue reaction scores in the minimal or slight range throughout the study. There were no apparent differences between the test and control samples, or between the reactions elicited by the baseline (ERF 89-0711) and the 12-month station samples.

14. PROLENE (Polypropylene) Suture, Dyed, 6-0, Stability Study No. 783 A, B, C, D Baseline: ETO/N_2: Tissue Reaction (ERF 90-0210)

Report Date: 10/30/90
Test Article: PROLENE suture, size 6-0, dyed, sterilized by an experimental ethylene oxide/nitrogen process (test sample), or by the ETHICON production ethylene oxide/freon sterilization process (control sample).
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. The median tissue reaction scores for the test samples were in the minimal and slight range throughout the study. There were no apparent differences among the test and control samples.

15. PROLENE (Polypropylene) Suture, Dyed, 6-0, Stability Study No. 783 A & B12- Month Station: Tissue Reaction (ERF 91-0261)

Report Date: 8/14/91

Test Article: PROLENE suture, size 6-0, dyed, sterilized an experimental ethylene oxide/nitrogen process (test sample), or by the ETHICON production ethylene oxide/freon sterilization process (control sample), stored in production packaging at ambient conditions for a period of 12 months
Results: Samples were implanted into the gluteal muscles of rats for a period of 3, 28, or 91 days. The test sample elicited median tissue reaction scores in the slight range throughout the study. The control sample elicited median tissue reaction scores in the minimal to slight range. There were no obvious differences between the baseline (ERF 90-0210) and the 12-month station samples.

H. IMMUNOTOXICITY: Not done

I. ACUTE TOXICITY: Not done

J. SUBCHRONIC TOXICITY

1. Ninety Day Feeding Studies in Rats of a Diet Containing 5% Copper Phthalocyanine - Color Additive for Polypropylene Sutures (NDA 16-374; Vol. 1.1)

Report Date: 3/26/65
Test Article: Copper phthalocyanine
Results: Dietary administration of 5% copper phthalocyanine to rats for 90 days resulted in no evidence of systemic toxicity.

K. REPRODUCTIVE TOXICITY: Not done

L. CHRONIC TOXICITY

1. Study of Tissue Reaction to Colorless and Pigmented Monofilament, Polypropylene Suture in the Rat, the Rabbit and the Dog (NDA 16-374; Vol. 1.1)

Report Date: 3/10/64
Test Article: PROLENE suture, sizes 2-0 and 5-0, undyed and dyed
Results: *Rats (One-Year Interim)*: PROLENE suture, sizes 2-0 and 5-0, was implanted in muscle and subcutis. Samples were explanted at 3, 6, 9, or 12 months postimplantation. *Rabbits*: PROLENE suture, size 5-0 was implanted in the palpebral conjunctiva and explanted at 3, 5, 7, 10, 30, or 60 days postimplantation. *Dogs (3- Month Interim)*: PROLENE suture, sizes 2-0 and 5-0, was implanted in muscle and explanted (one dog) at 90 days postimplantation. Overall, no appreciable tissue damage was observed. The characteristic reaction was a narrow fibrous capsule. No differences in tissue reaction were observed between the clear and pigmented sutures.

2. Biological Behavior of Copper Phthalocyanine - Pigmented and Colorless Monofilament Polypropylene Sutures in the Ocular Tissues of the Rabbit (NDA 16-374; Vol. 1.1)

Report Date: 7/25/64
Test Article: PROLENE suture, size 5-0, undyed and dyed
Results: PROLENE suture was implanted into rectal dorsal muscle and palpebral conjunctiva, and explanted at 3, 7, 30, or 60 days postimplantation. Overall, no appreciable tissue damage was observed, and the characteristic reaction was slight chronic inflammation.

M. CARCINOGENICITY

1. Two Year Study of Tissue Reaction to Colorless and Pigmented Monofilament Polypropylene Sutures in the Rat (NDA 16-374; Vol. 1.1)

Report Date: 10/14/65
Test Article: PROLENE suture, sizes 2-0 and 5-0, undyed and dyed

Results: PROLENE suture was implanted into muscle and subcutis of rats. Explants were carried out at varying times postimplantation up to and including 24 months. From 18 months, the tissue reaction was minimal, characteristic of a relatively nonirritating foreign body, and similar to that observed at one year. No evidence of carcinogenicity was observed and the implants appeared intact.

2. Two Year Study of Tissue Reaction to Colorless and Pigmented Monofilament Polypropylene Sutures in the Dog (NDA 16-374; Vol. 1.1)

Report Date: 10/14/65
Test Article: PROLENE suture, sizes 2-0 and 5-0, undyed and dyed, EO sterilized
Results: PROLENE suture was implanted in the latissimus dorsi muscle of dogs, explanted at 3 months (one dog) and 2 years (3 dogs) postimplantation. Tissue reaction was slight and consisted of a fibrous capsule. This reaction was similar between the undyed and dyed samples, and was similar to that observed at 3 months. There was no evidence of carcinogenicity and the suture appeared intact.